L5 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1004748 CAPLUS Full-text
DN 143:306348
TI Preparation of pyrrolobenzodiazepinone derivatives as antitumor agents
IN Howard, Philip Wilson; Gregson, Stephen John
PA Spirogen Limited, UK
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005085251	A1	20050915	WO 2005-GB768	20050301

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI	GB 2004-4575	A	20040301
	GB 2004-26392	A	20041201

OS MARPAT 143:306348
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = labile leaving group, alkenyl or substituted phenyl; R2 and R5 independently = H, OH, SH, etc.; R3 and R4 independently = H, NH2, halo, etc. or the compound is a dimer with each monomer being of formula I, where the R3 and R4 groups of each monomer form together a dimer bridge -X-R-X-; R = alkylene group, which may be interrupted by heteroatoms or aromatic rings; X = O, S or NH; R6 = carbamate-based N-protecting group; R7 = oxygen protecting group or OH or R6 and R7 together form double bond between N10 and C11] and their pharmaceutically acceptable salts, are prepared and disclosed as antitumor agents. Thus, e.g., II was prepared by palladium catalyzed coupling of III (preparation given) with trans-propenylboronic acid followed by deprotection. The in vitro cytotoxicity of I towards K562 human chronic myeloid leukemia cells was evaluated using ELISA assay and it was revealed that selected compds. of the invention displayed IC50 values of less than 1 μM. I should prove useful in the treatment of proliferative diseases such as leukemia. Pharmaceutical compns. comprising I are disclosed.

IT 260544-29-4P 260544-30-7P 489475-06-1P
692760-70-6P 692760-72-8P 692760-74-0P
692760-76-2P 692760-78-4P 692760-80-8P
692760-82-0P 692760-86-4P 864754-68-7P
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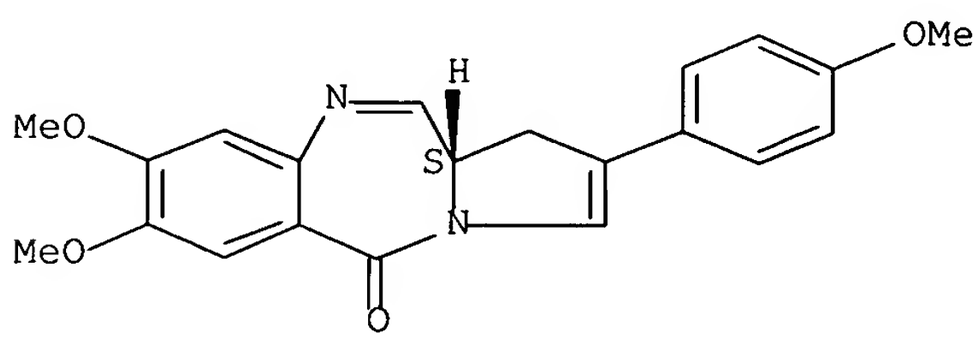
864754-95-0P 864754-96-1P 864754-97-2P
864754-98-3P 864754-99-4P 864755-00-0P
864755-01-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(preparation of pyrrolobenzodiazepinone derivs. as antitumor agents)

RN 260544-29-4 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(4-methoxyphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

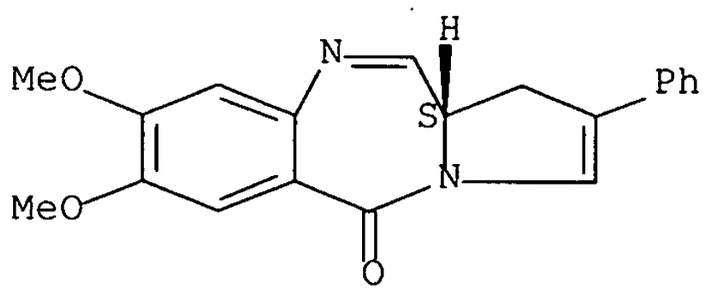
Absolute stereochemistry.



RN 260544-30-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-phenyl-, (11aS)- (9CI) (CA INDEX NAME)

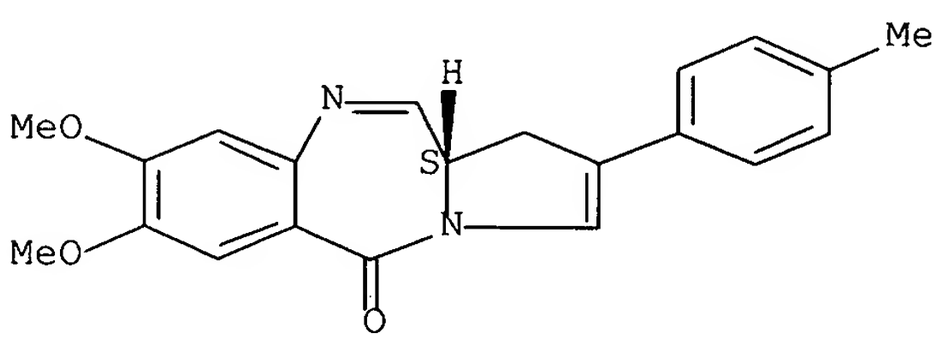
Absolute stereochemistry.



RN 489475-06-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(4-methylphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

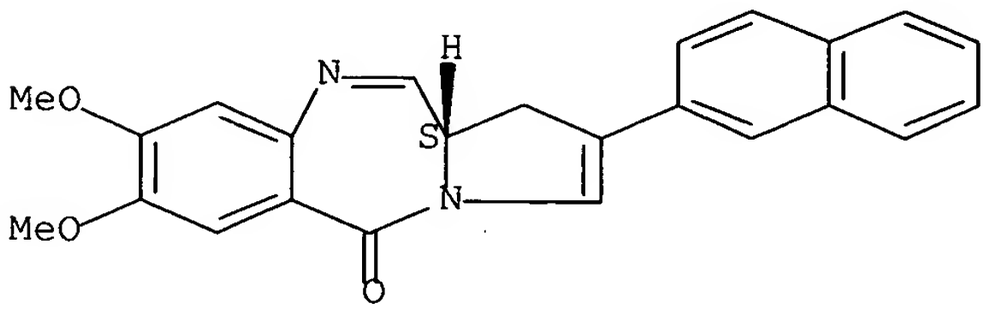
Absolute stereochemistry.



RN 692760-70-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(2-naphthalenyl)-, (11aS)- (9CI) (CA INDEX NAME)

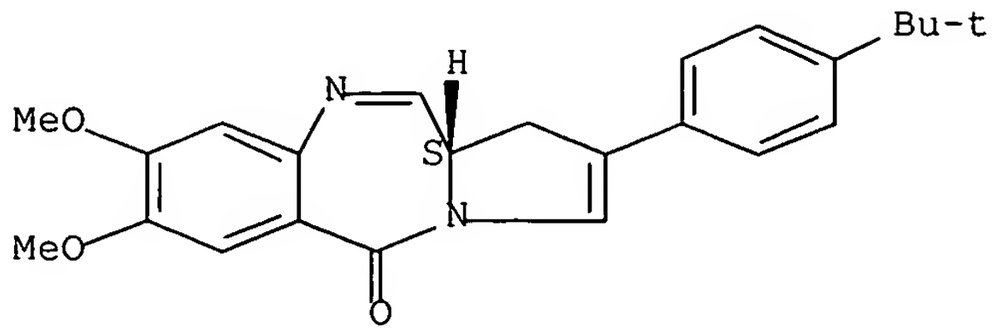
Absolute stereochemistry.



RN 692760-72-8 CAPLUS

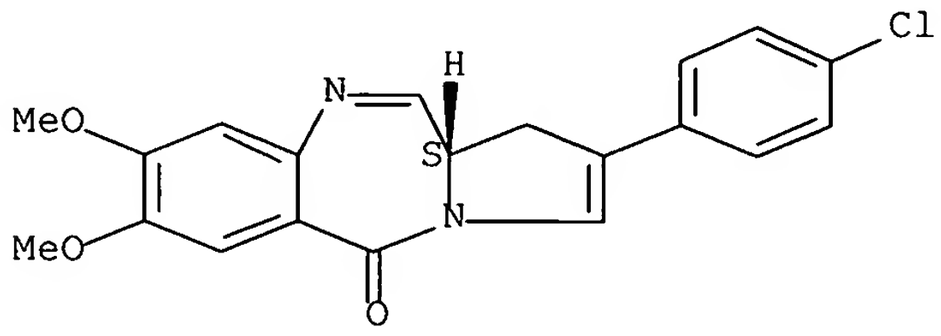
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-[4-(1,1-dimethylethyl)phenyl]-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



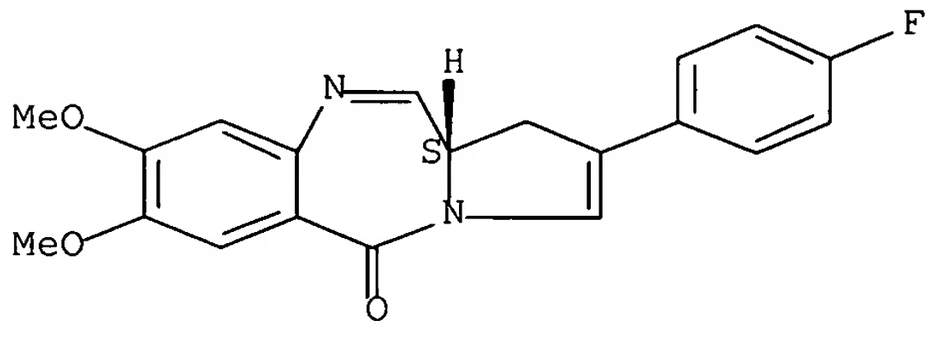
RN 692760-74-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(4-chlorophenyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



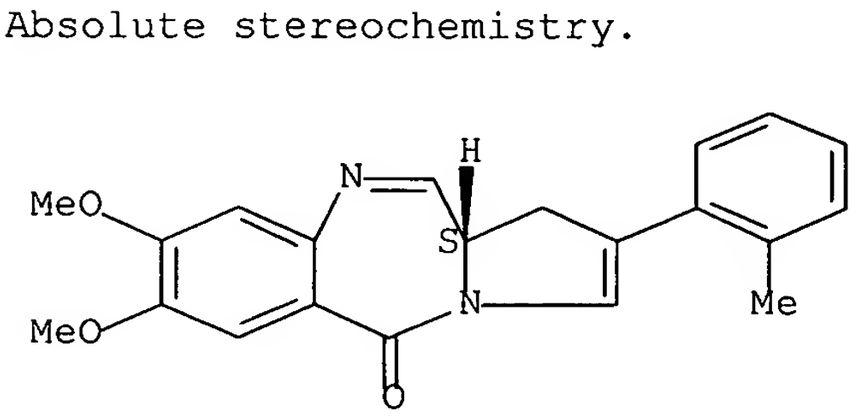
RN 692760-76-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(4-fluorophenyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



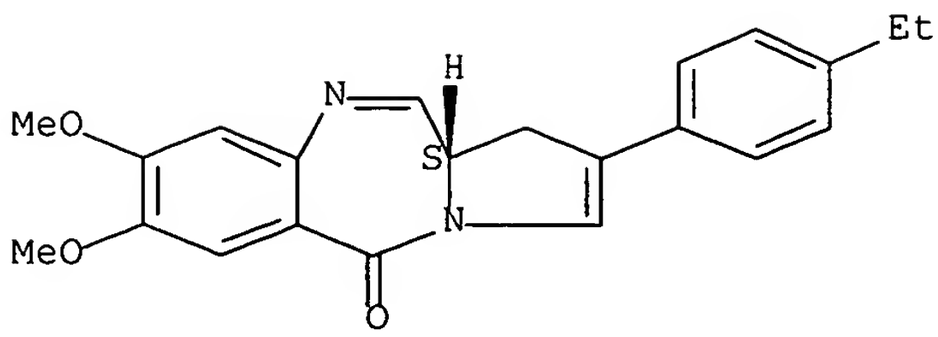
RN 692760-78-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(2-methylphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



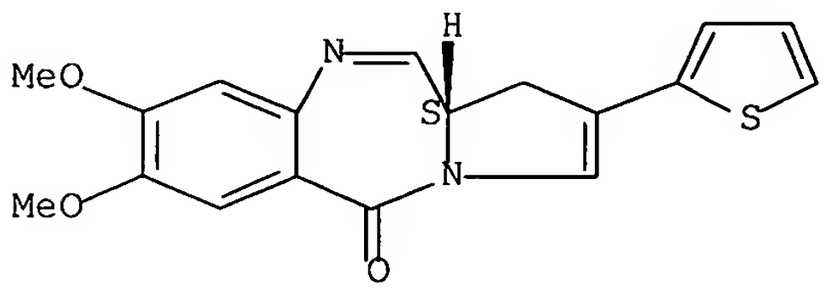
RN 692760-80-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(4-ethylphenyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



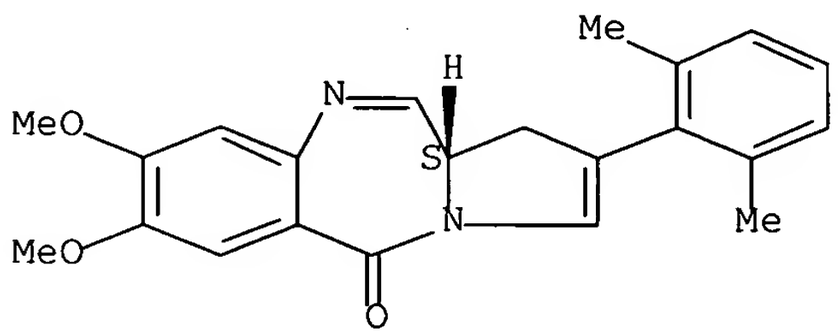
RN 692760-82-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(2-thienyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 692760-86-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(2,6-dimethylphenyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 864754-68-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,11a-dihydro-7-methoxy-2-(4-methoxyphenyl)-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

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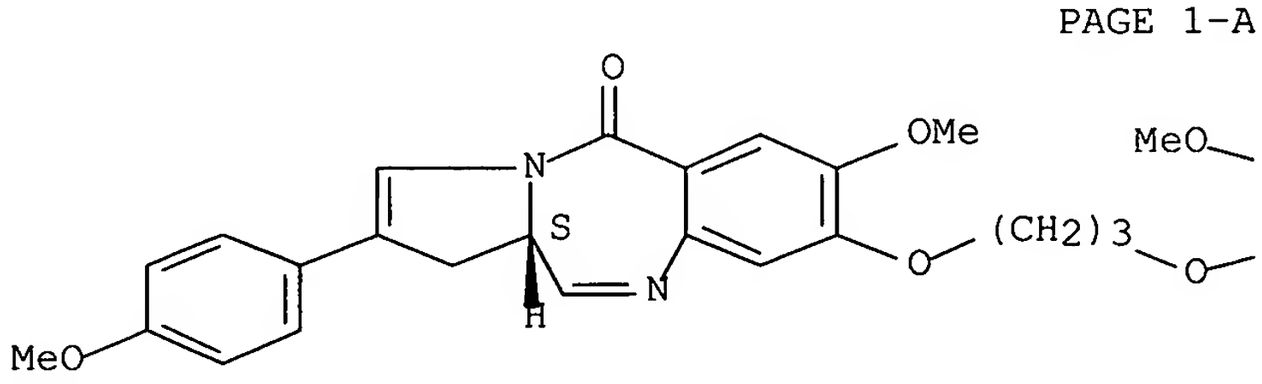
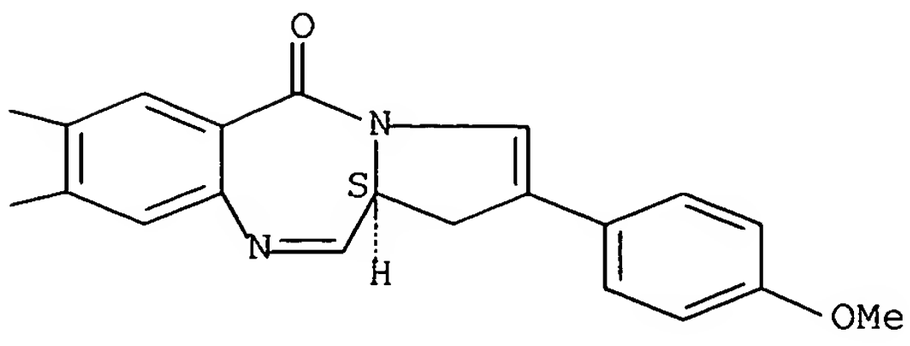
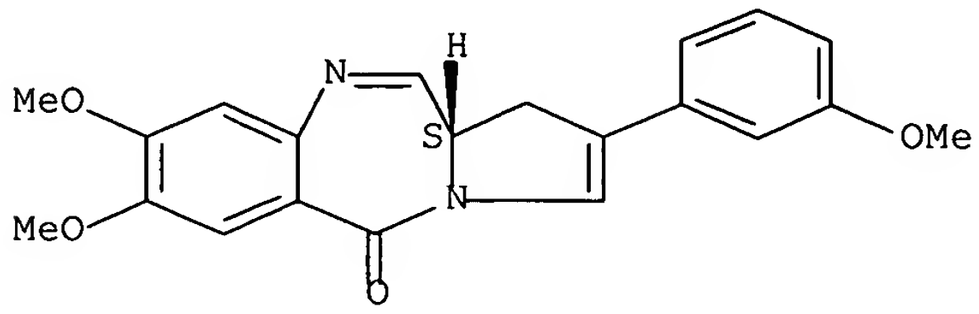


PAGE 1-B



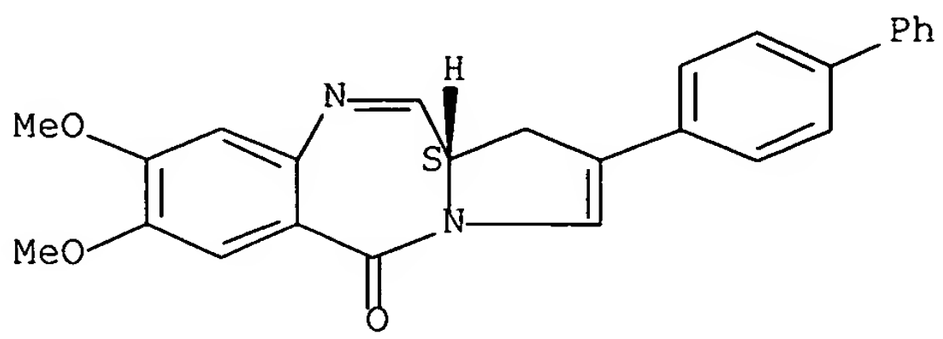
RN 864754-77-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(3-methoxyphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



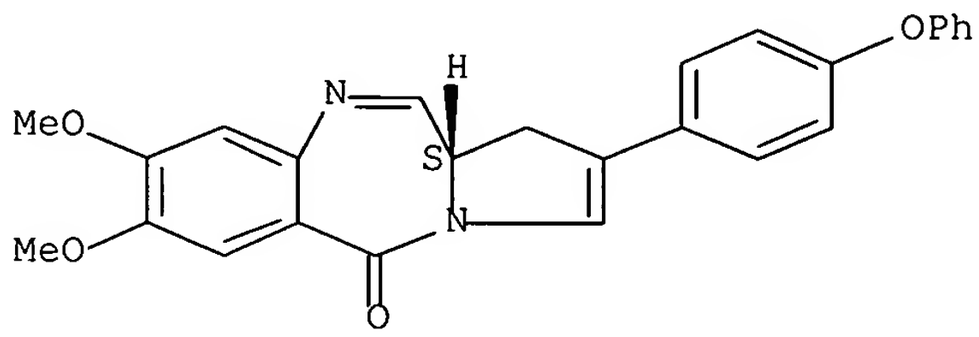
RN 864754-78-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-[1,1'-biphenyl]-4-yl-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



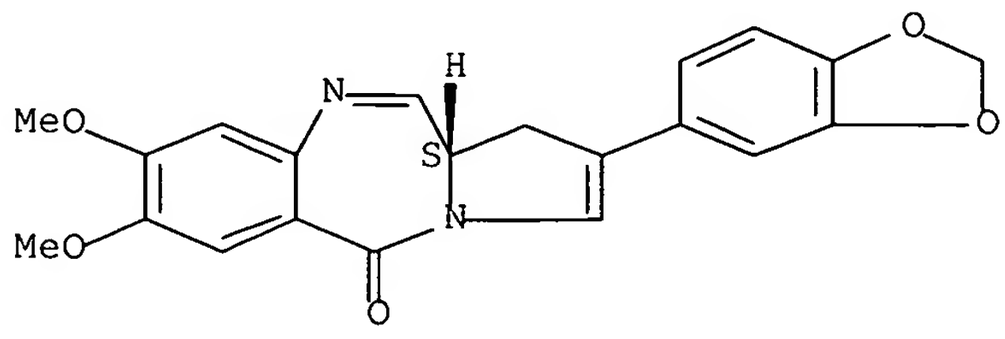
RN 864754-79-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(4-phenoxyphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



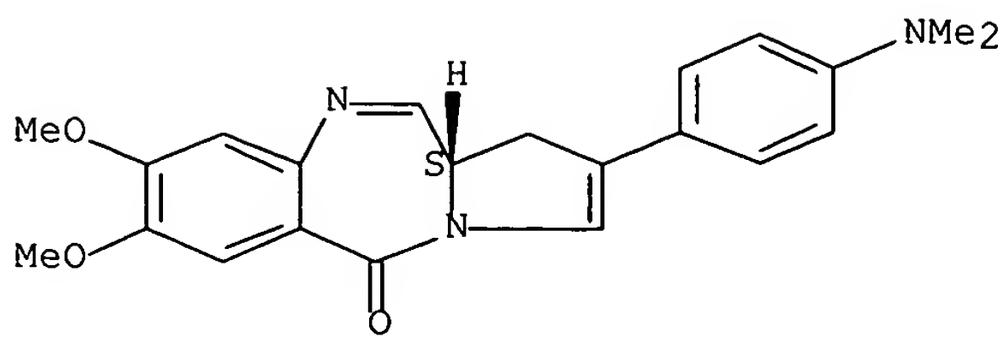
RN 864754-80-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(1,3-benzodioxol-5-yl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



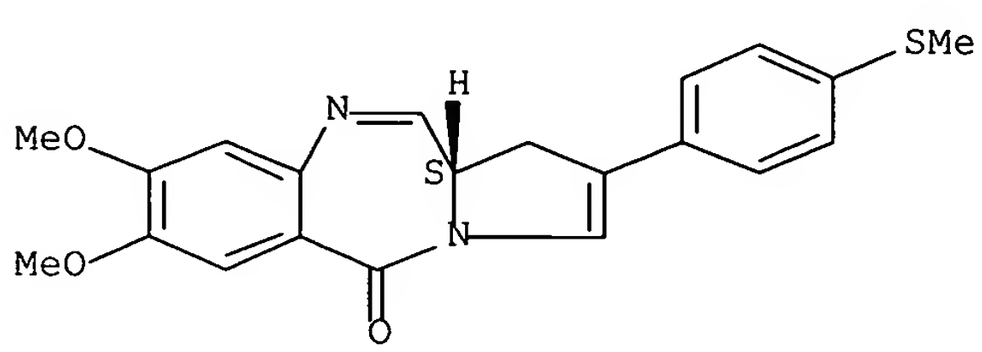
RN 864754-82-5 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-[4-(dimethylamino)phenyl]-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



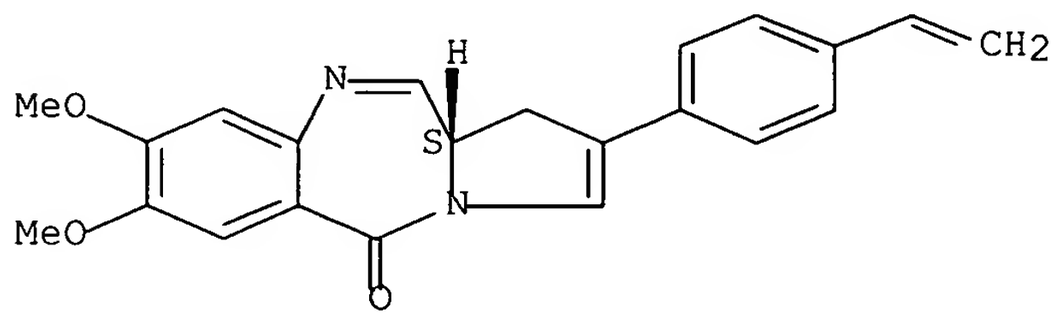
RN 864754-83-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-[4-(methylthio)phenyl]-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



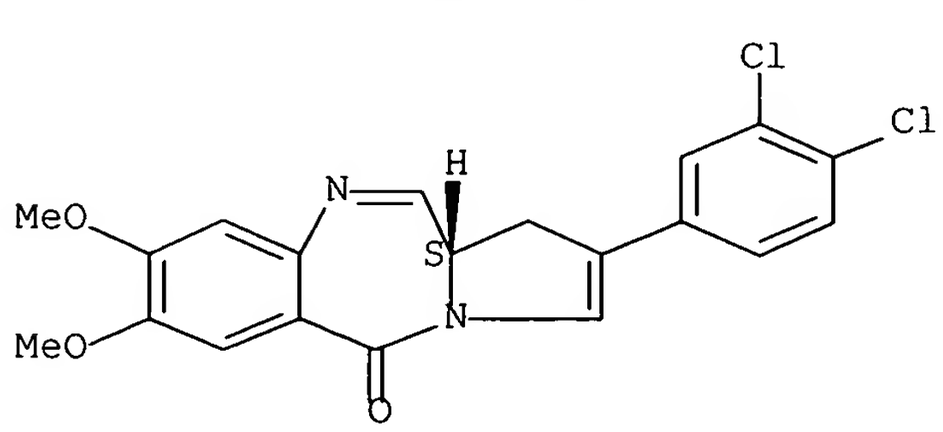
RN 864754-84-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(4-ethenylphenyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



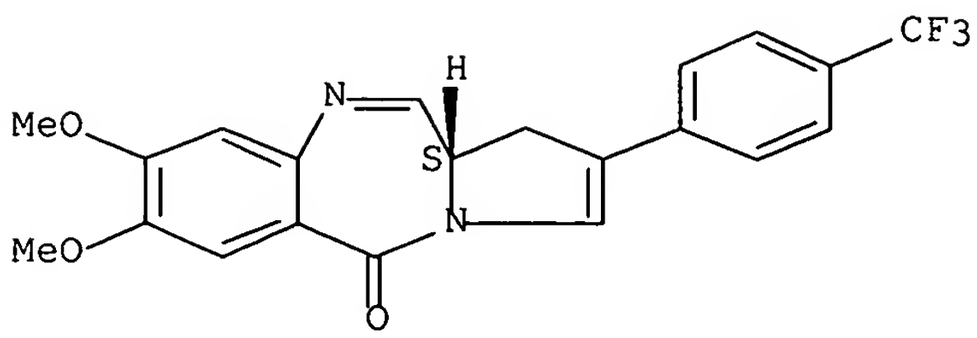
RN 864754-85-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(3,4-dichlorophenyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



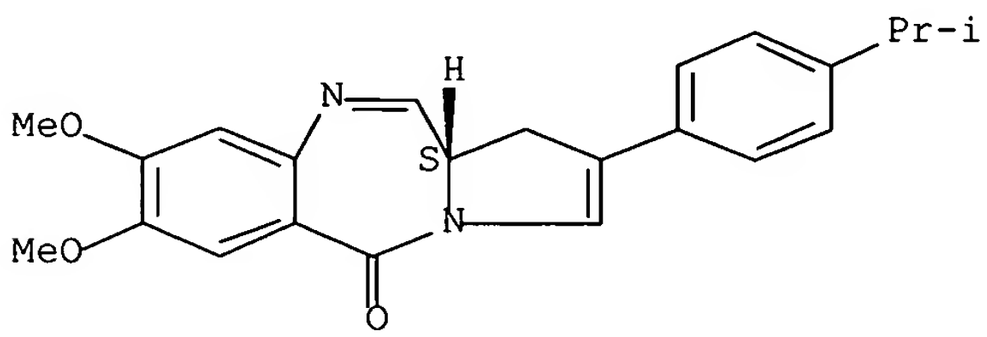
RN 864754-86-9 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-[4-(trifluoromethyl)phenyl]-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



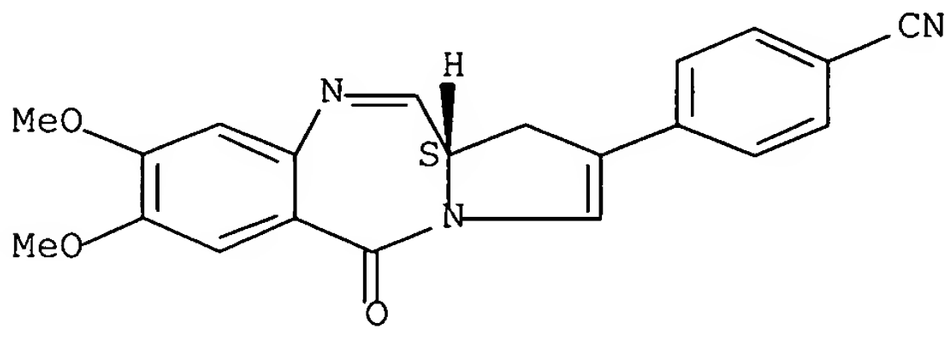
RN 864754-87-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-[4-(1-methylethyl)phenyl]-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



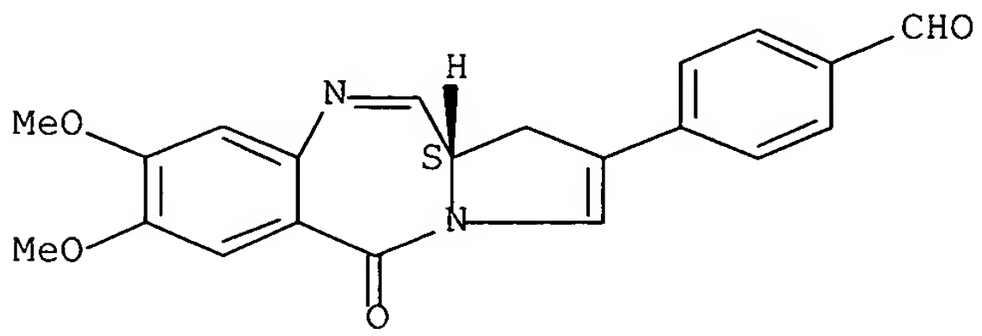
RN 864754-88-1 CAPLUS
CN Benzonitrile, 4-[(11aS)-5,11a-dihydro-7,8-dimethoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



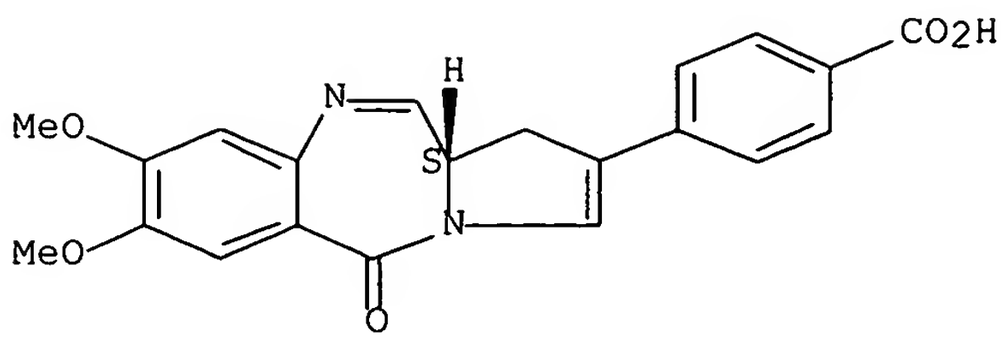
RN 864754-91-6 CAPLUS
CN Benzaldehyde, 4-[(11aS)-5,11a-dihydro-7,8-dimethoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



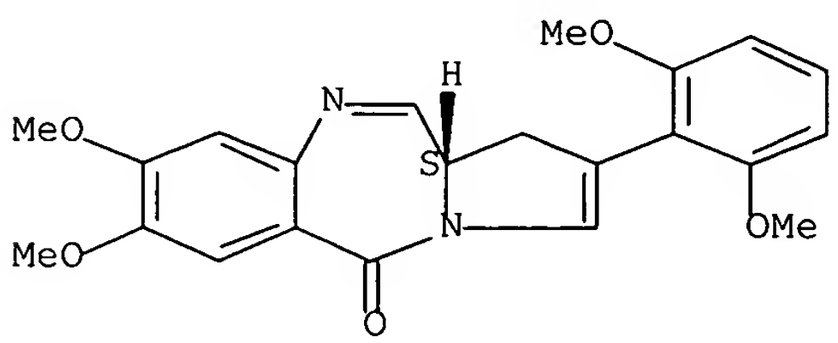
RN 864754-92-7 CAPLUS
CN Benzoic acid, 4-[(11aS)-5,11a-dihydro-7,8-dimethoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



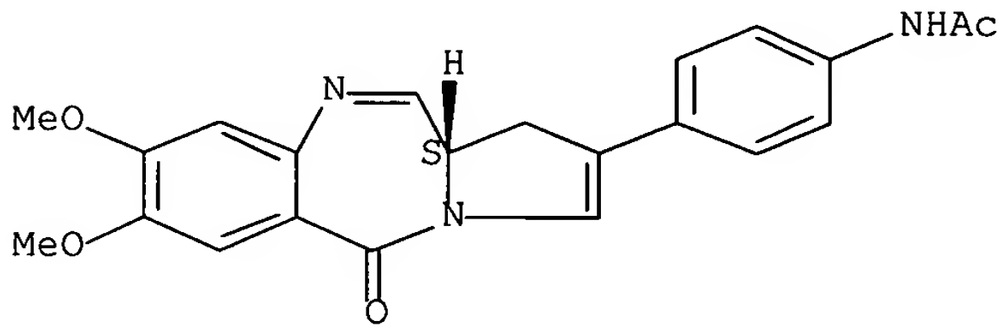
RN 864754-93-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(2,6-dimethoxyphenyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



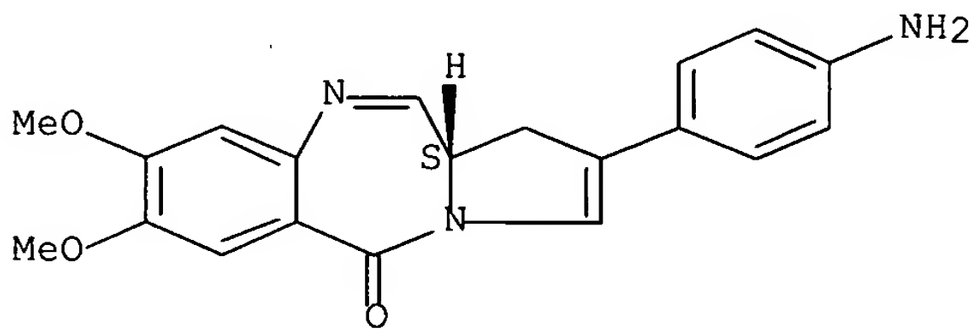
RN 864754-94-9 CAPLUS
CN Acetamide, N-[4-[(11aS)-5,11a-dihydro-7,8-dimethoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



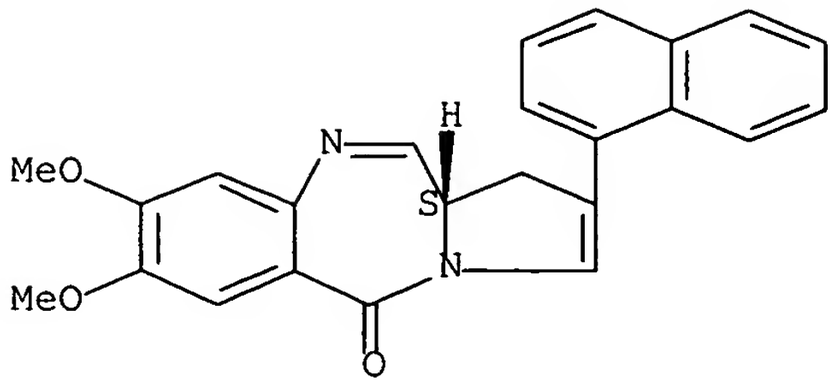
RN 864754-95-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(4-aminophenyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



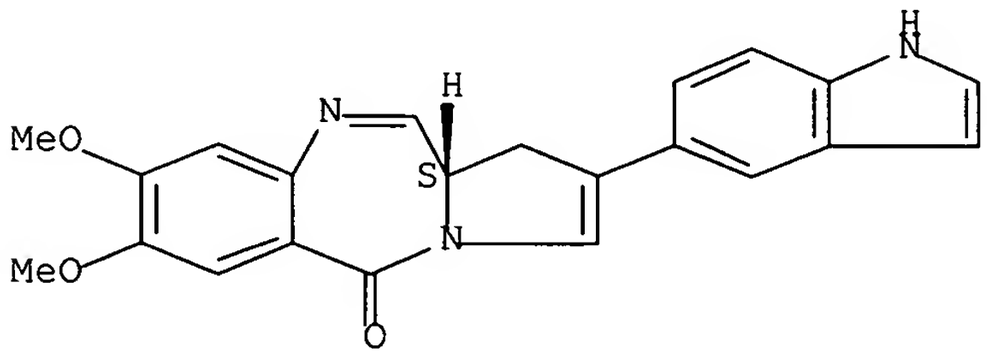
RN 864754-96-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(1-naphthalenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



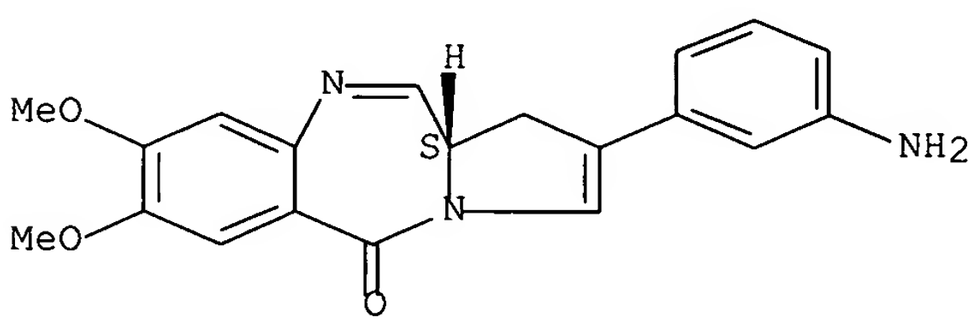
RN 864754-97-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-2-(1H-indol-5-yl)-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



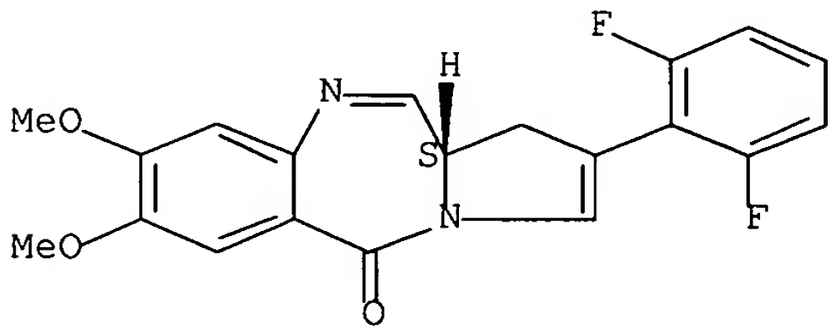
RN 864754-98-3 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(3-aminophenyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



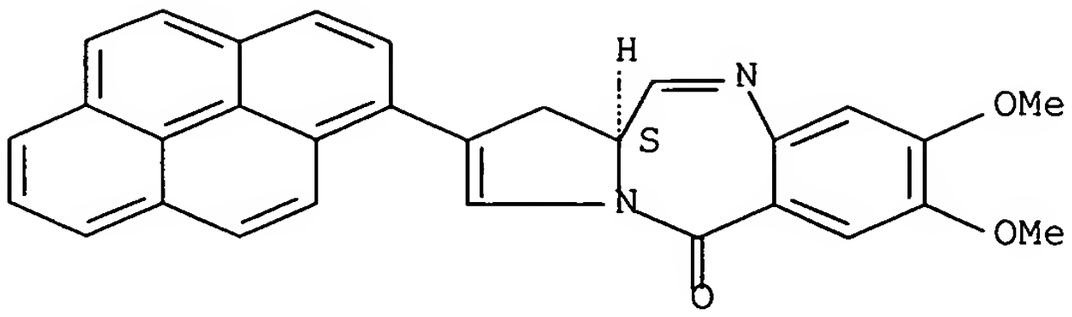
RN 864754-99-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(2,6-difluorophenyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



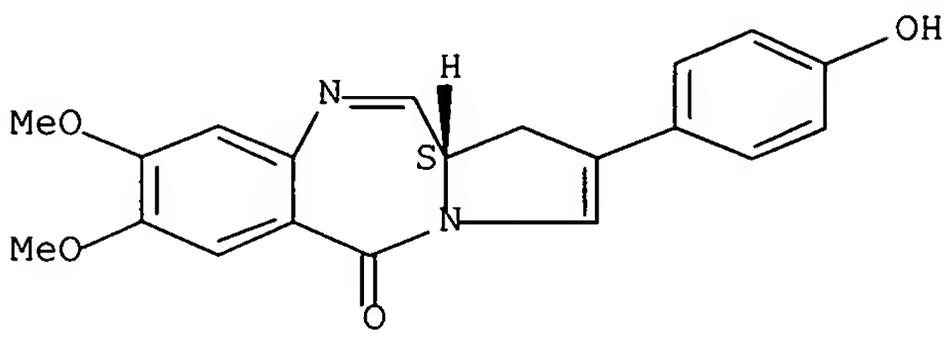
RN 864755-00-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(1-pyrenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



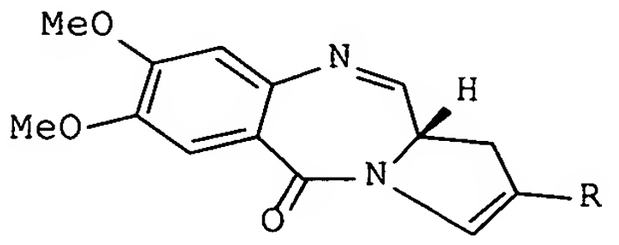
RN 864755-01-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-2-(4-hydroxyphenyl)-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

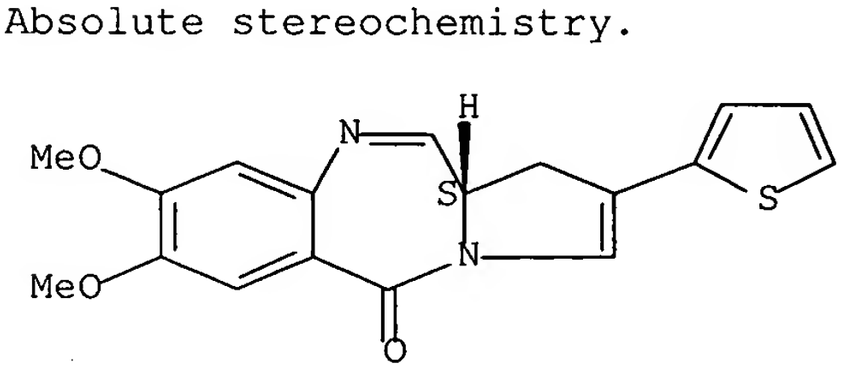
L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:767272 CAPLUS Full-text
DN 141:410907
TI Application of the Stille coupling reaction to the synthesis of C2-substituted endo-exo unsaturated pyrrolo[2,1-c][1,4]benzodiazepines (PBDs)
AU Tiberghien, Arnaud C.; Hagan, David; Howard, Philip W.; Thurston, David E.
CS Cancer Research UK Gene Targeted Drug Design Research Group, Department of Pharmaceutical and Biological Chemistry, The School of Pharmacy, London, WC1N 1AX, UK
SO Bioorganic & Medicinal Chemistry Letters (2004), 14(20), 5041-5044
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 141:410907
GI



I

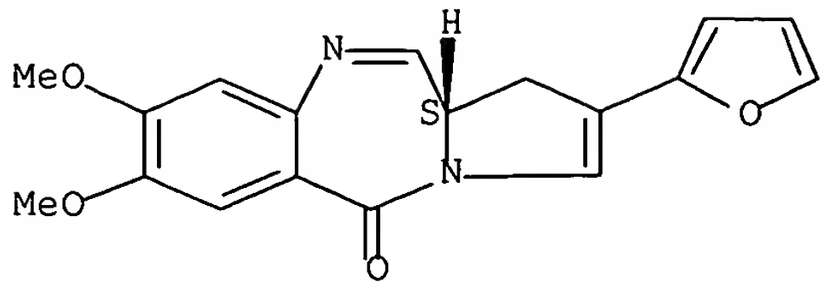
AB The Stille coupling reaction has been used to introduce novel vinyl, alkynyl, and heterocyclic substituents to the C2-position of pyrrolo[2,1-c][1,4]benzodiazepine dilactams. Sodium borohydride reduction followed by N10-SEM deprotection has provided five analogs I (R = H, CH2:CH, 2-thienyl, C.tplbond.CPh, 2-furyl) that contain C2-endo/exo-unsatn. and novel C2-substituents. These analogs have significant multilog cytotoxicity profiles in the NCI 60-Cell Line screen, and provide new SAR data for the PBD family.
IT 692760-82-0P 692760-84-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of C2-substituted endo-exo unsatd. pyrrolo[2,1-c][1,4]benzodiazepines via Stille coupling reaction and subsequent reduction/deprotection)
RN 692760-82-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(2-thienyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 692760-84-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(2-furanyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



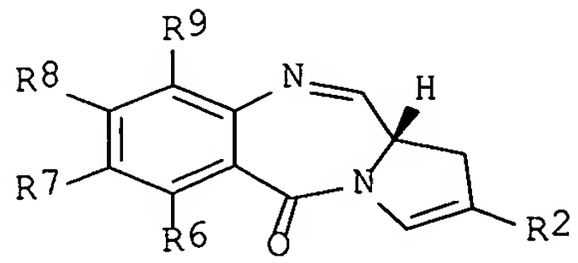
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

App's

L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:430806 CAPLUS Full-text
DN 140:423715
TI Preparation of pyrrolobenzodiazepines as anticancer agents agents
IN Thurston, David Edwin; Howard, Philip Wilson
PA Spirogen Limited, UK
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004043963	A1	20040527	WO 2003-GB4963	20031114
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2505489	AA	20040527	CA 2003-2505489	20031114
	AU 2003282251	A1	20040603	AU 2003-282251	20031114
	EP 1575955	A1	20050921	EP 2003-773870	20031114
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003016241	A	20051004	BR 2003-16241	20031114
	CN 1735616	A	20060215	CN 2003-80108373	20031114
	JP 2006507313	T2	20060302	JP 2004-550845	20031114
	US 2006128693	A1	20060615	US 2005-534825	20051020
PRAI	GB 2002-26593	A	20021114		
	WO 2003-GB4963	W	20031114		

OS MARPAT 140:423715
GI



I

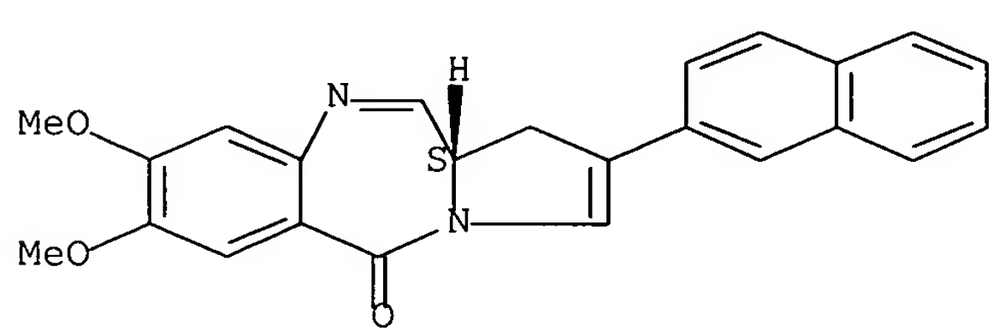
AB The title compds. (I), salts, solvates, chemical protected forms, and prodrugs thereof, [R6-R9 = H, R, OH, OR, SH, SR, NH2, NHR, NHRR', nitro, Me3Sn, halo (where R, R' = optionally substituted C1-7 alkyl, C3-20 heterocyclyl, or C5-20 aryl); or the compound is a dimer with each monomer being of formula I, where the R8 groups of each monomers form together a dimer bridge having the formula -X-R''-X- linking the monomers (where R" = C3-12 alkylene, which chain may be interrupted by one or more heteroatoms, e.g. O, S, NH, and/or aromatic rings, e.g. benzene or pyridine, and each X = O, S, or NH); or any pair of adjacent groups from R6 to R9 together form a group -O-(CH2)p-O- (where p = 1, 2); R2 = (i) optionally substituted naphthyl, (ii) optionally substituted thiophenyl or furanyl, or (iii) Ph substituted by: (a) one or more Cl or F, (b) Et or n-Pr, (c) 4-tert-Bu, or (d) 2-Me; or (e) two Me groups in the 2- and 6-positions] are prepared Also disclosed are (1) the use of the compound I in the manufacture of a medicament for treating a proliferative disease and (2) a method of treatment of a proliferative disease, comprising administering to a

subject in need of treatment a therapeutically-effective amount of the compound I. Thus, (11aS)-5,10,11,11a-tetrahydro-7,8-dimethoxy-10-[2-(trimethylsilyl)ethoxymethyl]-2-[[(trifluoromethyl)sulfonyl]oxy]-5,11- dioxo-1H-pyrrolo[2,1-c][1,4]benzodiazepine was coupled with 4-ethylbenzeneboronic acid in the presence of tetrakis(triphenylphosphine)palladium(0) and Na2CO3 in a mixture of EtOH, H2O, and benzene at room temperature for 41 h to give I (R6 = R9 = H, R6 = R7 = OMe, R2 = 4-ethylphenyl) (II). II showed IC50 of <0.1 μg/mL for inhibiting the proliferation of breast MACL MCF7, renal RXF 955L, and melanoma MEXF 462NL cancer cells.

IT 692760-70-6P, (11aS)-1,11a-Dihydro-7,8-dimethoxy-2-(2-naphthyl)-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one 692760-72-8P, (11aS)-1,11a-Dihydro-7,8-dimethoxy-2-(4-tert-butylphenyl)-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one 692760-74-0P, (11aS)-1,11a-Dihydro-7,8-dimethoxy-2-(4-chlorophenyl)-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one 692760-76-2P, (11aS)-1,11a-Dihydro-7,8-dimethoxy-2-(4-fluorophenyl)-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one 692760-78-4P, (11aS)-1,11a-Dihydro-7,8-dimethoxy-2-(2-methylphenyl)-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one 692760-80-8P, (11aS)-1,11a-Dihydro-7,8-dimethoxy-2-(4-ethylphenyl)-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one 692760-82-0P, (11aS)-1,11a-Dihydro-7,8-dimethoxy-2-(thiophen-2-yl)-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one 692760-84-2P, (11aS)-1,11a-Dihydro-7,8-dimethoxy-2-(2-furyl)-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one 692760-86-4P, (11aS)-1,11a-Dihydro-7,8-dimethoxy-2-(2,6-dimethylphenyl)-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolobenzodiazepines as anticancer agents)

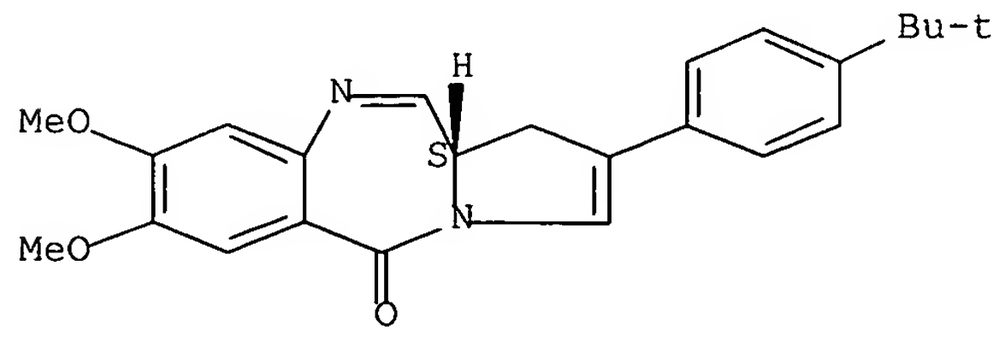
RN 692760-70-6 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(2-naphthalenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



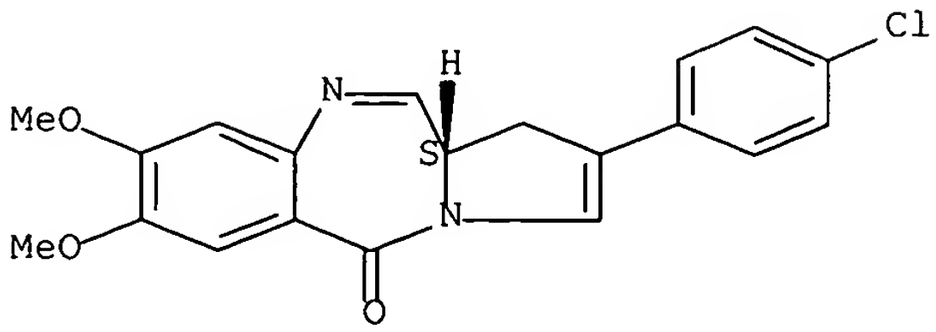
RN 692760-72-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-[4-(1,1-dimethylethyl)phenyl]-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



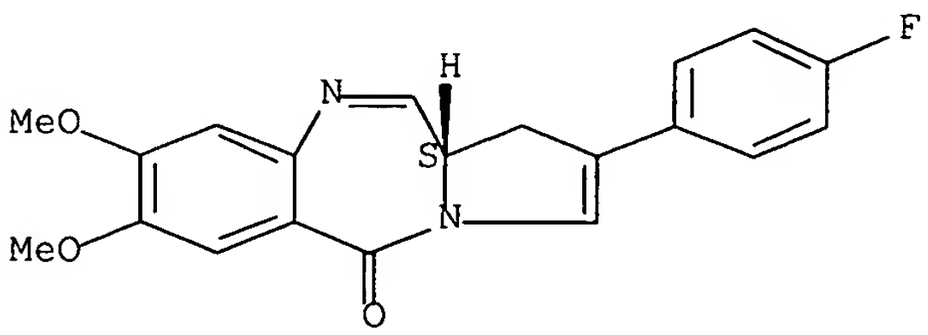
RN 692760-74-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(4-chlorophenyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



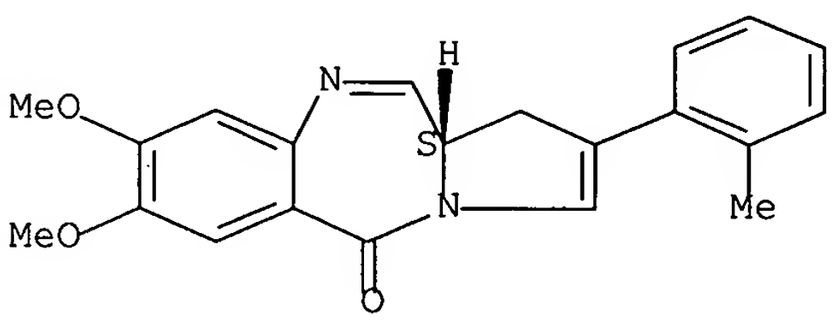
RN 692760-76-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(4-fluorophenyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



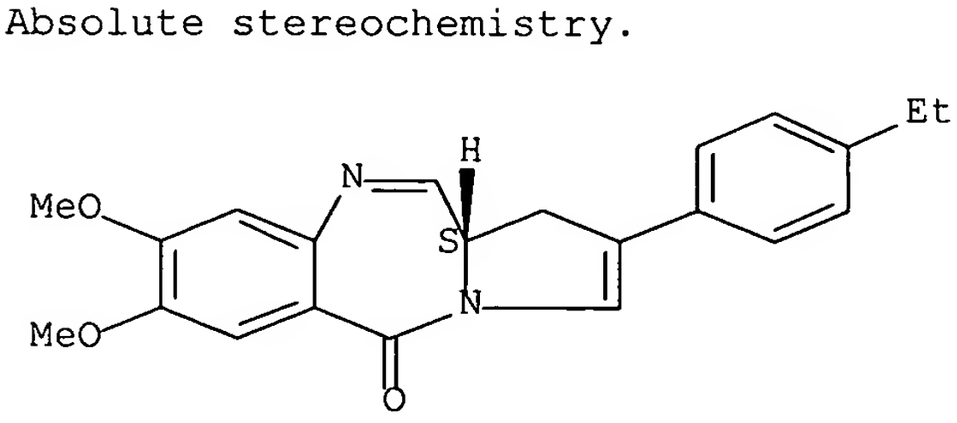
RN 692760-78-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(2-methylphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



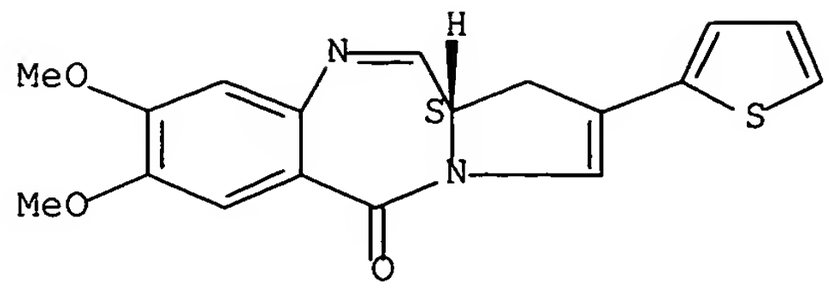
RN 692760-80-8 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(4-ethylphenyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



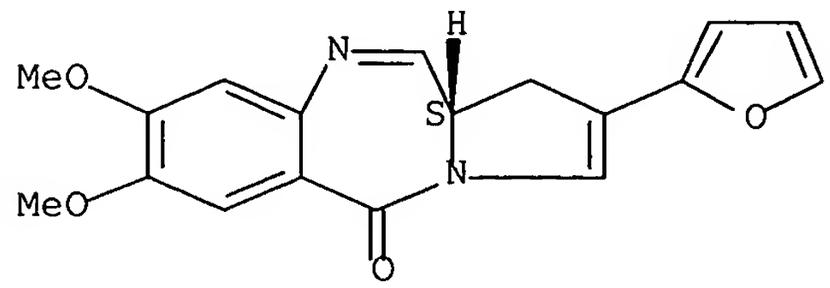
RN 692760-82-0 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(2-thienyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



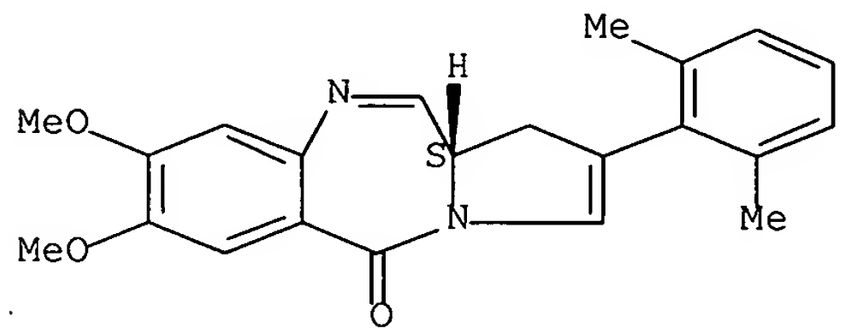
RN 692760-84-2 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(2-furanyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 692760-86-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-(2,6-dimethylphenyl)-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

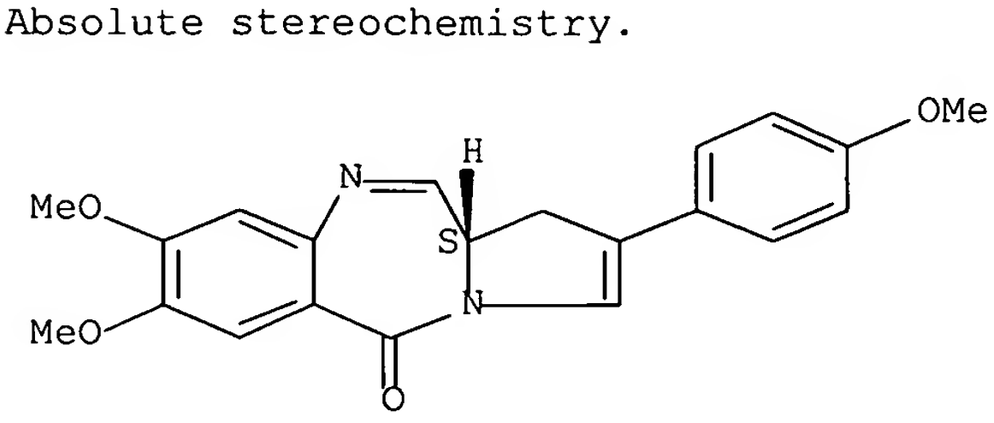
Absolute stereochemistry.



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

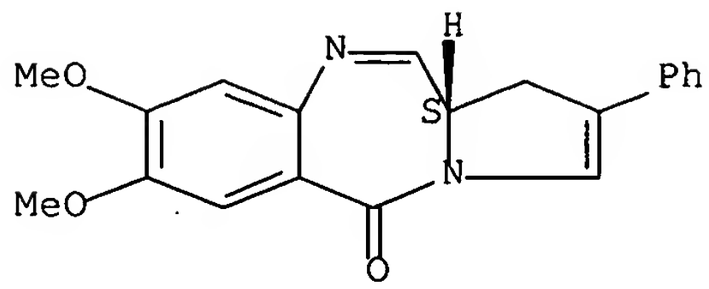
L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:557716 CAPLUS Full-text
DN 138:122628
TI Synthesis of novel C2-aryl pyrrolobenzodiazepines (PBDs) as potential antitumor agents
AU Cooper, Nectaroula; Hagan, David R.; Tiberghien, Arnaud; Ademefun, Temitope; Matthews, Charles S.; Howard, Philip W.; Thurston, David E.
CS CRUK Gene Targeted Drug Design Research Group, School of Pharmacy, University of London, London, WC1N 1AX, UK
SO Chemical Communications (Cambridge, United Kingdom) (2002), (16), 1764-1765
CODEN: CHCOFS; ISSN: 1359-7345
PB Royal Society of Chemistry
DT Journal
LA English
OS CASREACT 138:122628
AB Three novel C2-aryl substituted pyrrolobenzodiazepines (PBDs) have been synthesized and evaluated in a number of cell lines revealing selective cytotoxicity at the sub-nanomolar level towards melanoma and ovarian cancer cell lines. Compds. thus prepared included (11aS)-1,11a-dihydro-7,8-dimethoxy-2-phenyl-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one, (11aS)-1,11a-dihydro-7,8-dimethoxy-2-(4-methylphenyl)-5H-pyrrolo[2,1- c][1,4]benzodiazepin-5-one and (11aS)-1,11a-dihydro-7,8-dimethoxy-2-(4- methoxyphenyl)-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one. (11AS)-1,2,3,11a-tetrahydro-7,8-dimethoxy-5H-pyrrolo[2,1- c][1,4]benzodiazepin-5-one was also screened against cancer cell lines.
IT 260544-29-4P, (11aS)-1,11a-Dihydro-7,8-dimethoxy-2-(4-methoxyphenyl)-5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one
260544-30-7P, (11aS)-1,11a-Dihydro-7,8-dimethoxy-2-phenyl-5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one 489475-06-1P, (11aS)-1,11a-Dihydro-7,8-dimethoxy-2-(4-methylphenyl)-5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of C2-aryl pyrrolobenzodiazepines as potential antitumor agents)
RN 260544-29-4 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(4-methoxyphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



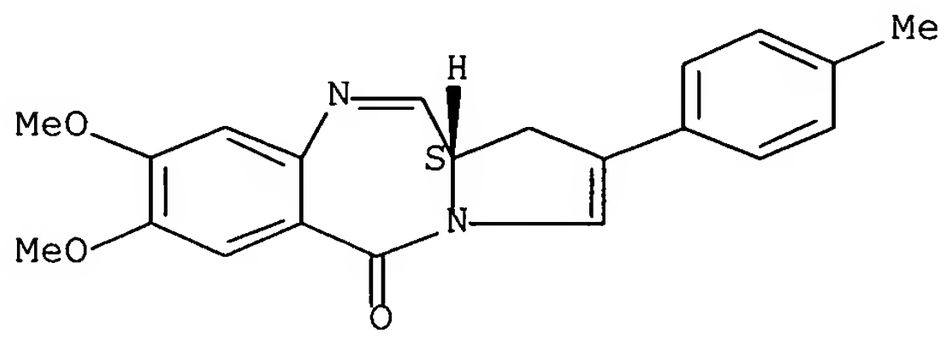
RN 260544-30-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-phenyl-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 489475-06-1 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(4-methylphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:161284 CAPLUS Full-text
DN 132:207851
TI Preparation of pyrrolobenzodiazepines (PBDs) as antitumor agents
IN Thurston, David Edwin; Howard, Philip Wilson
PA The University of Portsmouth Higher Education Corporation, UK
SO PCT Int. Appl., 258 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000012508	A2	20000309	WO 1999-GB2838	19990827
	WO 2000012508	A3	20000921		
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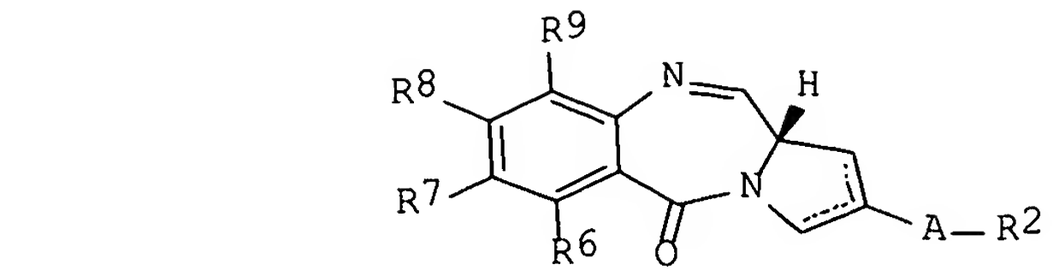
GI



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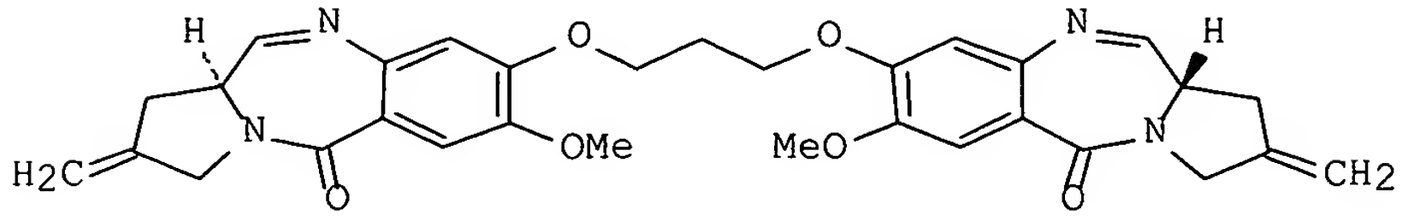


II

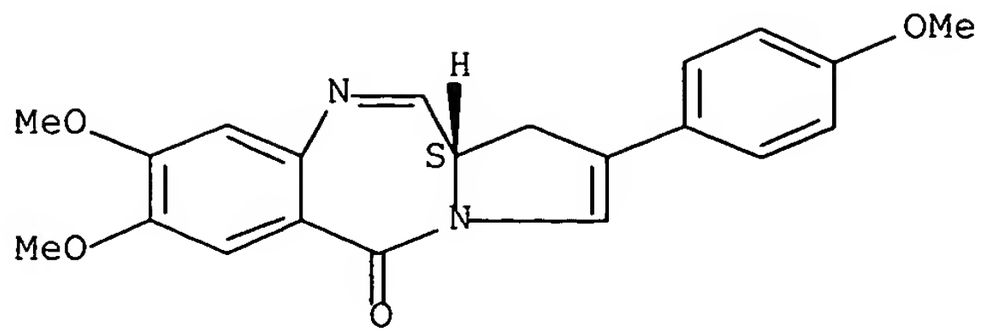
AB 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one derivs. (I) [wherein A = CH2 or a single bond; R = (un)substituted (ar)alkyl, (ar)alkenyl, or (ar)alkynyl; R2 = R, OH, OR, CO2H, CO2R, COH, COR, SO2R, CN; R6, R7, R8, and R9 = independently H, R, OH, OR, halo, NH2, NHR, NO2, SnMe3; or the compound is a dimer with each monomer being the same or different and being of formula I and the R8 groups of the monomers form a -X-R'-X- bridge, where R' is an alkylene chain which may contain ≥ 1 heteroatoms and/or aromatic rings and/or carbon-carbon double or triple bonds, and each X = independently O, S, or N] were prepared for the treatment of gene-based diseases, e.g. neoplastic diseases and Alzheimer's disease, and also bacterial, parasitic, and viral infections. For example, II was synthesized in a 6-step sequence. 1',3'-Bis(4-carboxy-2-methoxy-5-nitrophenoxy)propane (preparation given) was bisamidated with (2S)-2-(tert-butyldimethylsilyloxymethyl)-4-methylenepyrrolidine (74%). TBAF-mediated cleavage of the silyl protecting groups (94%), followed by reduction of the nitro groups by NH2NH2 in the presence of Raney Ni (63%) and N-acylation with allyl chloroformate (50%), gave the protected diamine. Ring closure was accomplished under Swern oxidation conditions, (COCl)2-DMSO and TEA, (32%). Finally, the imine was formed from the carbinolamine by N-deprotection using Pd(PPh3)4 and elimination of H2O (77%). Both large scale in vitro cytotoxicity cell screens and and in vivo hollow fiber and human tumor xenograft assays were performed on selected compds. of the invention. For instance, II exhibited potent and selective cytotoxicity against the lung cancer cell line NCI-H460, the colon cell line HCC-2998, the CNS cancer cell line SNB-75, and the melanoma cell lines MALME-3M (very potent, 0.08 μM) and UACC-62 (very potent, 0.07 μM). In human xenograft studies against five types of tumors, II demonstrated anticancer activity with mixed toxicity results. In addition, II was shown to be the most potent DNA-stabilizing agent known to date according to a DNA helix melting temperature assay. The IC50 value for II in the A2780 human ovarian carcinoma cell line was only 23 pM, a 320-fold increase in cytotoxicity compared to the known antitumor agent DSB-120 (IC50 = 5.2 nM). Remarkably, II was also almost 9000-fold more potent in the cisplatin-resistant A2780cisR cell line (IC50 = 24 pM) than DSB-120 (IC50 = 0.21 mM), suggesting that II may have potential in the treatment of cisplatin-refractory disease.

IT 260544-29-4P, UP 2092 260544-30-7P, UP 2095
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of 5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one antitumor agents from 2-amino- or 2-nitrobenzoic acid derivs. and pyrrolidines)

RN 260544-29-4 CAPLUS

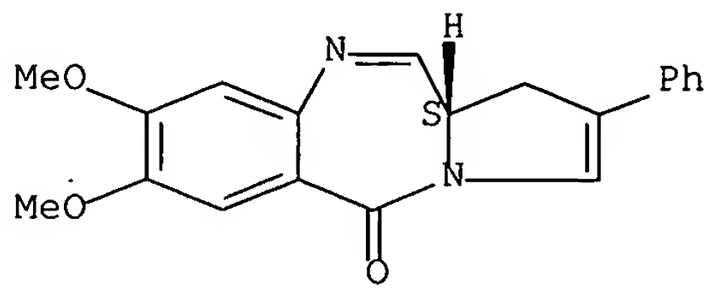
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-(4-methoxyphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 260544-30-7 CAPLUS
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-7,8-dimethoxy-2-phenyl-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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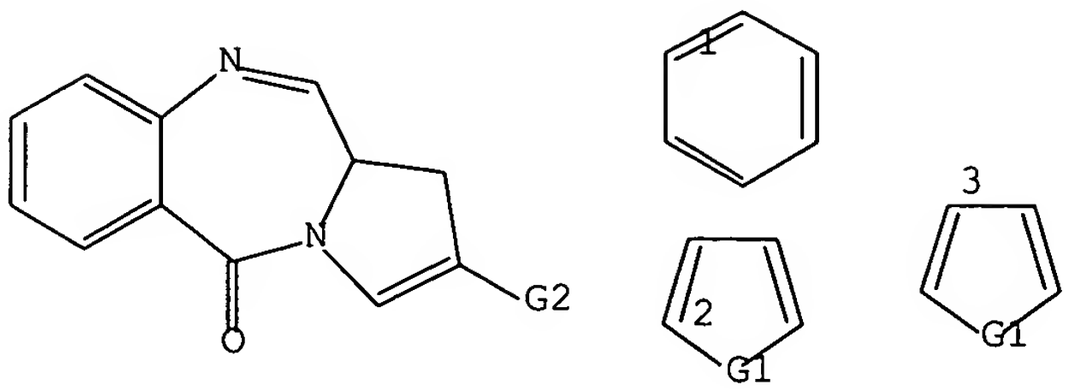


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 G2 [@1],[@2],[@3]

Structure attributes must be viewed using STN Express query preparation.
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L2                QUE L1
L3              2 S L2
L4             35 S L2 FUL

      FILE 'CAPLUS' ENTERED AT 20:12:51 ON 31 AUG 2006
L5              5 S L4


COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                    26.01     193.16

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
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CA SUBSCRIBER PRICE                                    -3.75      -3.75

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